



NORMATIVE DATA OF NASAL MUCOCILIARY CLEARANCE TIME IN HEALTHY INDIAN POPULATION - A PRELIMINARY STUDY

Otolaryngology

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| Manish Verma | Senior resident Department of Otorhinolaryngology, BPS Govt. Medical College for Women, Khanpur Kalan, Sonapat, Haryana, India |
| Jyoti Yadav | Professor and Head Department of Physiology, Pt.BD Sharma Postgraduate Institute of Medical Sciences, Rohtak, Haryana, India |
| Uma Garg | Professor and Head Department of Otorhinolaryngology, BPS Govt. Medical College for Women, Khanpur Kalan, Sonapat, Haryana, India |
| Jai Prakash Narayan | Postgraduate resident Department of Otorhinolaryngology, Pt.BD Sharma Postgraduate Institute of Medical Sciences, Rohtak, Haryana, India |
| Prikshit* | Postgraduate resident Department of Otorhinolaryngology, Pt.BD Sharma Postgraduate Institute of Medical Sciences, Rohtak, Haryana, India *Corresponding Author |

ABSTRACT

Nasal mucociliary clearance is a physiological defence mechanism of nasal cavity and it depends upon the nasal secretion and ciliary movement. The mucociliary system comprises of wave like beating of cilia of mucosal cells and movement of thin overlying mucus blanket with its entrapped particles towards the nasopharynx. This gets affected in abnormalities of cilia as well as the mucus and it is determined to obtain an in vivo measurement of the effectiveness of the interaction between the them. Various techniques are employed for measuring NMC namely saccharin test and tests using dyes or radio labeled particles. Saccharin test, an inexpensive, simple, reproducible and non-invasive method was used in this study in 200 healthy subjects. The mean value of nasal mucociliary clearance obtained was 7.25 ± 0.20 minutes (range 5.5-17.5 minutes). It was 7.20 ± 0.38 in males and 7.11 ± 0.26 in females. There was no statistical difference between the two genders ($p > 0.05$).

KEYWORDS

Nasal mucociliary clearance time, Healthy volunteers, Saccharin test

INTRODUCTION:

The nose is not only the most prominent feature of the face but also respiratory inlet and, as such, is easily insulted by trauma and external hazardous environmental factors. The nose, an unpaired structure is divided sagittally into two chambers, however, it acts as a single functional unit. The chief functions of nose are olfaction, filtration, humidification, warming the inspired air and mucociliary clearance (NMC). As inspired air is conducted through the nose, its temperature and humidity is adjusted to normal body temperature. Further the particulate matter is removed by mucociliary action to render it safe for lower respiratory tract. These functions are performed by pseudostratified columnar ciliated epithelium and are supported by the underlying submucosal tissues. In certain areas such as the conchae, this is a complex structure of ciliary mucous membrane, glands, blood spaces and connective tissues based upon bone, and are under the control of the autonomic nervous system.¹

On account of large surface area (70 m^2) and continuous exposure to air (10^4 liters/ day), a normal person inhales approximately 10^{10} dust particles daily.² Many of these particles include pollen grains, bacteria, viruses, fungi, noxious gases, smoke and a variety of other environmental chemicals. The nose efficiently filters out most of the particles as small as $5 \mu\text{m}$.³ The mucociliary transport system of nose is of prime importance in this regard and is one of the most important defence mechanisms of the entire respiratory tract.³ This is an undisputed fact that the nose with its mucociliary mechanism, is nature's best air-conditioner.

The mucociliary system comprise of wave like beating of the cilia of the mucosal cells and movement of the thin overlying mucus blanket, with its entrapped particles, towards the nasopharynx, where it is either swallowed or spit out. The term mucus is used loosely to describe, what probably consists of the mixture of surface secretion from the mucosa i.e. glycoproteins, mucoproteins, enzymes, immunoglobulins, surface epithelial cells, leucocytes, water and ions.⁴ The mucus blanket is arranged in two layers for the mucociliary transport mechanism to be effective; a superficial viscid sheet (gel layer), moving over the underlying serous fluid (sol layer), which bathes the cilia and microvilli.⁵ The nasal mucus under normal conditions is produced at a rate of 0.1 to 0.3 mls/kg/day.⁶ The physical properties of the mucus particularly the viscoelasticity has important effect on mucociliary clearance.⁷ Several investigators have suggested that a decrease in

mucociliary clearance may result from change in flow properties of the mucus.⁸ The interaction between ciliary activity and mucus seems to be a function of the rheologic properties rather than the biochemical characteristics of mucus.⁹

Nasal secretions contain glycoproteins like sialomucins and sulfomucins, however, it mainly contains water. There are also ions, enzymes like lysozymes and lactoferrin, circulatory proteins like macroglobulin, immunoglobulins and cells (surface epithelium, basophil, eosinophil, leucocytes). Cilia found on the surface of the cells in respiratory tract propel the mucus backward towards the nasopharynx by beating in a metachronous fashion. Each cell contains around 200 cilia with approximate length of 5 micrometer and they beat with frequency of 10-20 Hz between 32-40 degree. There are two phases of ciliary movement i.e. rapid propulsive phase and slow recovery phase.^{10,11}

Abnormalities of mucociliary transport mechanism may be due to abnormal function of cilia or the mucus. The cilia may be reduced in number, have a slow rate of beating or beat not at all. Variations in the nature of mucus or in the anatomic and physiologic integrity of the cilia may be a result of disease, drug, or environmental influences e.g. oxygen deprivation, proteolytic enzyme action, bacterial toxins, noxious gases, chemicals and metals.³

The factors affecting the ciliary action include temperature (< 10 and > 45 degree celsius), drying, isotonicity of secretions, infection, pH (good function in slight alkaline medium) and drugs. Acetylcholine and adrenaline increase whereas propranolol decreases the NMC. Various tests to measure mucociliary clearance time includes: Quinian method, Andersen method and electron microscopy.¹²

NMC is the mirror image of bronchial mucociliary clearance¹³ and the ciliary beat frequency of nasal mucosa correlates with that of tracheal mucosa.^{14,15} NMC is influenced by physiological factors such as the amount of mucus produced; the ciliary beat efficiency; anatomic factors such as nasal airflow, patency of the sinus ostia in the prechambers and biochemical factors such as mucus composition. Impairment of NMC results in the accumulation of respiratory secretions and reduced lung defenses leading to infections and inflammation.¹⁵ As ciliary defects or impairment in mucociliary clearance might account for the high incidence of lower respiratory

tract infection. NMC thus functions as a biomarker and serve as an early warning system for susceptibility to respiratory diseases.¹⁶

Since there are no standalone NMC study in normal persons, hence this preliminary study, was undertaken to evaluate the NMC time in 200 healthy volunteers using Anderson's saccharin method to establish normative data of NMC for Indian population.

MATERIAL AND METHODS:

The present study was conducted in the department of Otorhinolaryngology and Physiology PGIMS, Rohtak on a total of 200 healthy volunteers of either sex between age group of 15-55 years in outpatient department by using (saccharin method) Anderson's method.¹⁷

EXCLUSION CRITERIA:

Smokers, passive smokers, tobacco chewers and snuff users were excluded from the study. Subjects who had local pathology such as deviated nasal septum, nasal polyps, nasal allergy, rhinosinusitis and upper respiratory infection. Similarly subjects with diabetes, chronic systemic diseases, bronchiectasis, valvular heart disease, bleeding diatheses, and persons on medication(s) particularly were also excluded, as above factors are known to affect NMC.

Saccharin test is a simple, non-invasive reproducible method while methods using radio labeled particles are time consuming, cumbersome and expensive.¹⁷

In the present study classical saccharine test was performed in sitting position. An approximately 1 mm diameter particle of saccharin was placed 1 cm behind the anterior end of the inferior nasal turbinate at the floor of nose. The subject was requested not to smoke, eat, drink, cough, or sneeze during the test. The test was repeated in the other nostril and the average of two sides was taken to obviate any effect of nasal cycle on NMC.

Volunteers were asked to report the change in taste as soon as it was perceived. The time from the placement of the saccharin particle to the initial perception of the sweet taste was taken as NMC time and was recorded in minutes. The test was terminated after 30 minutes if they didn't appreciate the change of taste. These volunteers were excluded from the study as it was presumed that there was some abnormality in taste perception which was verified by directly placing the saccharin particle on the tongue.¹⁷

RESULT:

A total of 200 healthy volunteers comprising of 100 males and 100 females of 15-55 years of age group were included in the study. The mean value of nasal mucociliary clearance obtained was 7.25 ± 0.20 minutes (range 5.5-17.5 minutes). It was 7.20 ± 0.38 in males and 7.11 ± 0.26 in females. There was no statistical difference between the two sexes ($p > 0.05$).

DISCUSSION:

Nose is responsible for a number of important functions, the most important is, it being part of airway with inherent protective function for the lower respiratory tract like humidification and cleaning the inspired air of pollutants. This function may be altered in diseases which can be assessed by study of nasal mucociliary clearance time.¹⁸

Various reports reveal an impaired mucociliary clearance in people with allergic tendencies, bronchial asthma, chronic rhinitis, sinusitis and women with prolonged biomass fuel exposure with the impaired clearance usually attributed to ciliary damage as well as altered secretions.¹⁹ There are various techniques to measure mucociliary clearance time i.e. Anderson's saccharin test, NMC time using colour dye, NMC time using combination of colour substance plus saccharin and using teflon disks and Gamma scintigraphy using ^{99m}Tc. Most of these techniques are time consuming, cumbersome and expensive.²⁰ Measurement of NMC using saccharin test serves as a good alternative, simple, inexpensive technique to measure NMC with good coefficient of repeatability.¹⁷ Normal value of NMC time is up to 20 minutes. If it is 21-30 minutes it is prolonged, 31-60 minutes is severely prolonged and over 60 minutes is grossly prolonged.¹³

Saccharin test is usually performed prior to referring patients for ciliary beat frequency estimation, as it is reported that all patients with primary ciliary dyskinesia have NMC >60 minutes, if correct

precautions are observed. The only disadvantage of this method is that the determination of transit time may be influenced by the taste threshold of the patient.²¹

Increased NMC time signifying a decline in mucociliary clearance could be attributed to a variety of anatomical, physiological, and biochemical changes occurring during the normal ageing process, which may affect the response of the lungs to inhaled agents.²² Anatomical changes that occur with ageing include nasal mucosal damage which has accumulated from infections over the years, altered proportions of elastic tissues and collagen. Physiological alterations that could impair mucociliary clearance include abnormally slow or uncoordinated ciliary beating where neighbouring cilia do not beat in a coordinated fashion and in the same direction. This could be the result of abnormal ciliary ultrastructure or occur de novo.²³

Passali et al.(1985) reported the normal values of nasal mucociliary clearance in healthy children was 9.96 minutes.²⁴ Yadav et al.(1999) studied nasal mucociliary clearance in 30 children of adenoiditis of either sex in age group of 6 to 14 years and 30 healthy controls. They reported the mean value of NMC was 8.18 ± 1.81 minutes (5.08-13.02 minutes) in healthy children.²⁵ Ranga et al.(2000) studied nasal mucociliary clearance in 50 children of either sex suffering from adenotonsillar hypertrophy and healthy controls in the age group of 6 to 14 years and they observed that the NMC time in healthy children was 8.55 ± 2.11 minutes (5.09 to 13.5 minutes).²⁶ Yadav et al.(2001) studied nasal mucociliary clearance in 100 healthy school children in the age group 4-15 years and they observed the mean value of NMC time was 5.7 ± 2.59 min in males and 6.37 ± 2.59 in females. The difference between males and females was not statistically significant ($p > 0.10$).²⁷ The NMC time reported in normal Indian children is lower as compared to European (Italian) children. This may be due to racial factors like configuration of skull.

Many authors have studied nasal mucociliary clearance in various diseases and conditions like chronic smokers²⁸, effect of irradiation on NMC in cases of head and neck cancer²⁹, allergic rhinitis³⁰ bronchial asthma³¹, passive smoking³², menstrual cycle³³ and bronchiectasis³⁴. In all the above studies they studied the controls (healthy subjects) also. The NMC time in above studies was 7 to 8.5 minutes. However the controls in the above studies varied from 25 to 30 persons. Hence it was planned to study NMC time in a reasonable number (200) of healthy subjects to establish normative data of healthy subjects in Indian population to act as bench mark for future studies. Further the present study is an ongoing process and we intend to study the same in more number of subjects to establish NMC time in healthy Indians.

The NMC time of the present study is comparable with most of the Indian studies including from our institution indicating that NMC time is constant irrespective of place of study.^{20,27} However, reported NMC time in literature is lower in children.¹⁶⁻¹⁹ The reported increased NMC in adults as compared to children may be due to normal ageing.¹⁵ Yadav et al studied the effect of ageing on nasal mucociliary clearance. They reported that ageing affects NMC especially after 60 years of age. Hence we studied the NMC time between 15-55 years³⁵.

The study highlights NMC time in 200 healthy volunteers. Preventive measures like health education will go a long way towards informing them about the risks of poor nasal and respiratory health and giving cautionary advice. This (Andersen method) standard, simple, quick, inexpensive, and noninvasive test can be used for periodic assessment of NMC and can therefore serve as an early diagnostic pointer and pave the way for recognizing the susceptibility to progression to diseases. However, most of the studies reported world over have studied 25-30 healthy subjects whereas we studied 200 healthy volunteers. Hence it is more authentic normative data for future reference on NMC time. However, we are studying more number of patients to authenticate the NMC time in healthy Indian population.

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